Canadian Agency for Drugs and Technologies in Health

RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

TITLE: Mindfulness Interventions for the Treatment of Post-Traumatic Stress Disorder, Generalized Anxiety Disorder, Depression, and Substance Use Disorders: A Review of the Clinical Effectiveness and Guidelines

DATE: 19 June 2015

CONTEXT AND POLICY ISSUES

Post-traumatic stress disorder (PTSD) is the recurring and intrusive recollection of an overwhelming traumatic event.[1] Individuals with PTSD relive the traumatic event in a variety of ways (e.g. memories, flashbacks, dreams), avoid stimuli associated with the event (e.g. places, people, thoughts, feelings, dissociation), and experience symptoms of increased arousal (e.g. difficulty sleeping, irritability, decreased concentration, hypervigilance).[1] A Canadian study based on a nationally representative sample of 3,006 adults reported that the prevalence rates of lifetime PTSD was estimated to be 9.2%, with one month prevalence rates of 2.4%.[2]Furthermore, it was estimated that 63.0%, 44.7%, and 41.3% of PTSD patients had major depression, substance abuse and dependence, and alcohol abuse and dependence, respectively.[2] The treatment for PTSD includes psychotherapy (e.g. exposure psychotherapy, supportive psychotherapy) and drug therapy.[1]

Generalized anxiety disorder (GAD) is a chronic and disabling disorder that is primarily characterized by excessive anxiety and uncontrollable worry about everyday life.[3,4] The patient must present with three out of the following six symptoms for a definitive diagnosis: restlessness, difficulty concentrating, sleep disturbances, irritability, muscle tension, and becoming easily fatigued.[3] Patients with GAD are often functionally impaired and can be significantly distressed due to their symptoms.[4] The onset of GAD tends to be gradual in nature, it can fluctuate in severity, and is generally both recurrent and chronic.[4] According to the International Psychopharmacology Algorithm Project, the 12-month prevalence of GAD ranges between 1.1% and 3.6% while the lifetime prevalence is estimated to range between 4.1% and 6.6%.[4] In Canada, the lifetime prevalence rate of GAD is 8.7%.[5] While GAD can be a pure and singular disorder,[6] it is most often observed alongside other co-morbid conditions such as panic disorder, health anxiety, obsessive-compulsive disorder, major depression, and phobic anxiety disorders.[7] GAD is associated with consuming a large proportion of health services as it is one of the most common mental health disorders encountered in primary medical care.[7]

Depression may refer to a mood state, a syndrome which is a constellation of symptoms and signs (e.g., major depression or minor depression), or a mental disorder that identifies a distinct clinical condition (e.g., unipolar major depression).[8] Symptoms of depression can include depressed mood, loss of interest or pleasure, change in appetite or weight, sleep disturbance, fatigue or loss of energy, neurocognitive dysfunction, psychomotor agitation or retardation, feelings of worthlessness or excessive guilt, and suicidal ideation and behavior.[8] Worldwide estimates of the proportion of people who are likely to experience depression in their lifetime range between approximately 4% and 10% for major depression, and between approximately 2.5% and 5% for low grade chronic depressive symptoms.[9] In Canada, the lifetime prevalence rate of major depression episodes is 11.3%.[5]

Substance use disorders include substance dependence and substance abuse.[10] The criteria for substance dependence is a pattern of drug and alcohol use leading to three or more of the following within the same 12-month period: tolerance, withdrawal, substance taken in larger amounts or over longer period than intended, persistent desire or unsuccessful efforts to modify use, great deal of time spent in activities necessary to obtain the substance, reduction in social, occupational, recreational activities, and continued drug and alcohol use despite knowledge of problems.[10] The criteria for substance abuse is a pattern of drug and alcohol use leading to one or more of the following within the same 12-month period: failure to fulfil major role obligations, recurrent use in physically hazardous situations, recurrent drug and alcohol-related legal problems, continued use despite having persistent or recurrent problems.[10] In Canada, the lifetime prevalence rate of substance use disorder is 21.6%.[5]

Mindfulness is an integrative, mind-body based approach that helps people change the way they think and feel about their experiences.[11] It is a way of paying attention to the present moment by using meditation, breathing techniques, and yoga. Mindfulness involves consciously bringing awareness to thoughts and feelings, without making judgments , allowing the individual to become less enmeshed and better able to manage them.[11] The objective of this review is to summarize the clinical effectiveness and guidelines for the use of mindfulness interventions for the treatment of PTSD, GAD, depression, and substance use disorders in adults.

RESEARCH QUESTIONS

What is the clinical effectiveness of mindfulness interventions for the treatment of adults with PTSD, GAD, depression, or substance use disorders?

What are the evidence-based guidelines regarding the use of mindfulness interventions for the treatment of adults with PTSD, GAD, depression, or substance use disorders?

KEY FINDINGS

There is evidence to suggest that mindfulness may be beneficial as a monotherapy or adjunctive therapy for treating depression. The effectiveness of mindfulness for treating PTSD, and GAD is unclear. One RCT of low methodological quality suggested that mindfulness intervention is more effective than treatment as usual in lowering risk of relapse to substance use and heavy drinking. Six evidence based guideline documents considered the use of mindfulness in clinical practice. Four guidelines for depression suggested that mindfulness may be useful in reducing relapse in patients with depression, to be used in the maintenance phase of major depression, or used during the continuation phase of treatment with patients at high risk for relapse. One guideline suggested that mindfulness may be considered for adjunctive

treatment of hyperarousal symptoms, although there is no evidence that these are more effective than standard stress inoculation techniques. Another guideline suggested that mindfulness can be used to treat problematic drug and alcohol use problems by suitably trained and experienced drug and alcohol professionals.

METHODS

Literature Search Methods

A limited literature search was conducted on key resources including Ovid Medline, Ovid PsycINFO, PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2005 and May 21, 2015.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults with post-traumatic stress disorder (PTSD), generalized anxiety disorder (GAD), depression, or substance use disorders
Intervention	Mindfulness
Comparator	Other treatment for PTSD, GAD, depression, or substance use disorders No treatment
Outcomes	Q1: Symptom reduction, remission of the condition, increased quality of life. Q2: Evidence-based guidelines for the use of mindfulness for these disorders
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCTs), evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications or included in a selected systematic review/meta-analysis, or if the systematic reviews/meta-analyses or RCTs were published prior to 2013. Systematic reviews/meta-analyses with a more recent update were considered duplicates and were excluded; the most recent update was considered as the primary publication.

Critical Appraisal of Individual Studies

The methodological quality of the included systematic reviews and meta-analyses was evaluated using the AMSTAR checklist.[12] The Downs and Black Checklist was used to assess included RCTs,[13] and evidence-based guidelines were assessed with the AGREE II instrument.[14] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 502 citations were identified in the literature search. Following screening of titles and abstracts, 442 citations were excluded and 60 potentially relevant reports from the electronic search were retrieved for full-text review. 13 potentially relevant publications were retrieved from the grey literature search. Of these potentially relevant articles, 50 publications were excluded for various reasons, while 23 publications met the inclusion criteria and were included in this report. Four systematic reviews,[15-18] two meta-analyses,[19,20], eleven RCTs,[21-31] and six evidence-based guidelines[9,10,32-35] were included in this review. Appendix 1 describes the PRISMA flowchart of the study selection.

Appendix 6 presents a list studies that met the inclusion criteria but were published prior to 2013.

Summary of Study Characteristics

A summary of the characteristics of the included studies is provided in Appendix 2 and a detailed description of study interventions used in the included RCTs is provided in Appendix 5.

What is the clinical effectiveness of mindfulness interventions for the treatment of adults with PTSD, GAD, Depression, or substance use disorders?

Post-traumatic stress disorder

Three RCTs comparing mindfulness interventions with control groups in patients with PTSD were identified.[24,25,31] Two of these were conducted in Iran,[24,25] and one in the US.[31] All three studies included veterans diagnosed with PTSD.[24,25,31] Two of these studies compared mindfulness-based stress reduction with treatment as usual ,[25,31] and one study compared mindfulness-based stress reduction with no treatment.[24] Omidi et al. investigated the efficacy of mindfulness-based stress reduction on mood, emotional and behavioral function of veterans with PTSD.[25] Azad et al. investigated the effect of mindfulness-based stress reduction on the quality of life (QoL) of the veterans with PTSD,[24] and Kearny et al. investigated the efficacy of mindfulness-based stress reduction on PTSD symptoms, depression and QoL in veterans with PTSD.[31] All studies used a parallel-group design and sample sizes ranged from 32[24] to 62 participants.[25] Follow-up was conducted at 4 months in Kearny et al.,[31] at 2 months in Azad et al.[24] No follow-up was mentioned for Omidi et al.[25]

Depression

A total of 4 systematic reviews,[16,18-20] and five RCTs[21-23,26,27] comparing mindfulness interventions with control groups in patients with depression were identified. Three[18-20] of the systematic reviews were conducted in the UK and one[16] in the US. One systematic review by

Clarke et al.[19] included 7 RCTs comparing mindfulness-based cognitive therapy to any comparator in adults with full or partial remission from depression. The number of patients included in the trials ranged from 60 to 274. Another systematic review by Jain et al.[16] included 8 RCTs comparing mindfulness-based cognitive therapy to any comparator in adult patients suffering from depressive disorder. The number of patients included in the trials ranged from 18 to 219. Two of the trials using a mindfulness-based cognitive therapy intervention included in the systematic review by Jain et al.[16] were also included in the systematic review by Strauss et al.[20] The systematic review by Churchill et al.[18] included one RCT comparing acceptance and commitment therapy to a support group in adult patients with acute depression. The systematic review by Strauss et al.[20] included four trials assessing mindfulness interventions in patients with depression. Three of these trials used mindfulness-based cognitive therapy, and one trial used person-based cognitive therapy.

One RCT was conducted in each of the following countries: UK,[21] Australia,[22] Italy,[23] Netherlands,[26], and Canada[27]. Kuyken et al.[21] included adult patients with a diagnosis of recurrent major depression in full or partial remission. This study investigated the impact of mindfulness-based cognitive therapy on time to relapse or recurrence of depression, number of depression free days, and QoL when compared to maintenance antidepressant treatment. Meadows et al.[22] included non-depressed adults with a history of three or more episodes of depression investigating the impact of mindfulness-based cognitive therapy plus depression relapse active monitoring on the proportion of patients who relapsed or had a recurrence, days in major depressive episodes and time to relapse/recurrence when compared to depression relapse active monitoring alone. Chiesa et al.[23] included patients aged between 18 and 65 years diagnosed with major depression, single or recurrent episode, on treatment with antidepressants and failed to achieve remission. Chiesa et al.[23] investigated the impact of mindfulness-based cognitive therapy on major depression severity, anxiety, and QoL when compared to psychoeducation. Tovote et al.[26] included patients aged between 18 and 70 years with type 1 or 2 diabetes and having symptoms of depression. This RCT compared mindfulness-based cognitive therapy with cognitive behavior therapy or a waiting list for the reduction in depressive symptoms. Bedard et al.[27] included adult patients with symptoms of depression after a traumatic brain injury and compared mindfulness-based cognitive therapy to a waiting list for the reduction in depression symptoms.

Generalized anxiety disorder

One systematic review,[15] and two RCTs[29,30] assessing mindfulness interventions in patients with GAD were identified. The systematic review by Bolognesi et al.[15] was conducted in UK, while both RCTs[29,30] were conducted in the US. Bolognesi et al.[15] assessed the impact of mindfulness on anxiety and depression and included three studies using mindfulness-based cognitive therapy, three studies using mindfulness-based stress reduction and three studies using acceptance-based behavior therapy. Hayes-Skelton et al.[29] compared acceptance-based behavior therapy with applied relaxation in adult patients with principal diagnosis of GAD. Anxiety and QoL were assessed in this RCT. Hoge et al.[30] compared mindfulness-based stress reduction to stress management education in adult patients with current primary GAD. The impact of a mindfulness intervention on anxiety was assessed in this trial.

Substance use disorders

One systematic review,[17] and one RCT[28] assessing mindfulness interventions in patients with substance use disorder were identified. The systematic review by Chiesa and Serretti[17] was conducted in Italy and included 24 studies (14 RCTs and ten non-RCTs). Twelve studies focused on alcohol and/or heterogeneous substance use, four on cigarette smoking, three on

opiate use, one on marijuana use, and one on metamphetamine use. Eight studies focused on mindfulness-based stress reduction or related mindfulness-based interventions (MBIs), five on acceptance and commitment therapy, three on Spiritual self-schema therapy , two on Dialectical behavioral therapy, one study focused on a Vipassana meditation (where individuals assume a seated position and focus their attention onto the breath), one study focused on goal management training in adjunct to mindfulness meditation, and one study focused on a motivational intervention in adjunct to mindfulness meditation. Ten of the included studies compared MBIs to a waiting list, eight compared MBIs with an active treatment, two compared MBIs with non-specific educational interventions designed to be structurally equivalent to the MBIs. Bowen et al.[28] included adult patients enrolled in a substance abuse aftercare program. Mindfulness-based relapse prevention was compared to relapse prevention or treatment as usual in this RCT. Relapse to drug use and heavy drinking frequency of substance use in the past 90 days was assessed.

What are the evidence-based guidelines regarding the use of mindfulness interventions for the treatment of adults with PTSD, GAD, depression, or substance use disorders?

Post-traumatic stress disorder

The scope of the Management of Post-Traumatic Stress working group guidelines was to provide recommendations for the management of adult patients with PTSD.[34] The guidelines provided recommendations on screening, acute phase management, and treatment for PTSD. Recommendations were reported for pharmacotherapy, psychotherapy, somatic treatment, and complementary and alternative medicine which included mindfulness. The working group considered the following outcomes: QoL, morbidity/ mortality, patient satisfaction and PTSD symptoms.

Depression

The objective of the NICE guidelines was to provide practice advice on the care of adults with depression.[9] The guidelines provided recommendations on several interventions including psychological and psychosocial therapy, cognitive behavior therapy and mindfulness-based cognitive therapy. The authors considered the following outcomes: mortality/morbidity, treatment complications; rates of relapse, return to work, physical and social functioning, QoL, and costs. The SIGN guidelines targeted adult patients with depression, their caregivers, and health care providers.[33] The guidelines provided recommendations on self-help, structured exercise, and several psychological therapies including mindfulness-based cognitive therapy. The primary outcome was depression symptoms. Secondary outcomes included illness duration, relapse, QoL and patient satisfaction.

The Canadian Network for Mood and Anxiety Treatments (CANMAT) targeted adults with major depression.[32] The guidelines provided recommendations on several interventions including cognitive behavior therapy and mindfulness-based cognitive therapy. Outcomes were not explicitly reported in the guidelines.

The Management of Major Depressive disorder working group[35] targeted adult patients with major depression The guidelines provided recommendations on pharmacotherapy and psychotherapy interventions including acceptance and mindfulness. The authors considered the following outcomes: depressive symptoms, functional status, suicide risk, adverse effects, tolerability and adherence to treatment.

Substance use disorders

The New South Wales Department of Health guidelines[10] provided recommendations on cognitive behavior therapy, mindfulness based stress reduction, dialectical behavioral therapy, acceptance and commitment therapy, psychodynamic and interpersonal approaches, emotion regulation, and family approaches. The guidelines did not specify outcomes, but several co-morbidities were evaluated. These included depression, anxiety, psychosis, personal disorders, trauma, anger/aggression, pain and blood-borne viruses.

Summary of Critical Appraisal

A summary of the critical appraisal of individual studies is presented in Appendix 3.

What is the clinical effectiveness of mindfulness interventions for the treatment of adults with PTSD, GAD, Depression, or substance use disorders?

Post-traumatic stress disorder

All three RCTs for PTSD[24,25,31] had a small sample size (trials sample sizes ranged from 32[24] to 62[25]). The randomization method, allocation concealment, and blinding were not described in Azad and Zadeh[24]. In the RCT by Omidi et al.,[25] the randomization method was not described, and patients and investigators were not masked to treatment allocation. In the RCT by Kearney et al.[31] allocation was concealed, but the method used was not described. The randomization method was not described, and patients and investigators were not masked to treatment allocation.

Depression

A comprehensive literature search based on pre-defined criteria was used in all four systematic reviews.[16,18-20] The methodological quality were evaluated systematically and risk of bias of individual studies was assessed in the systematic reviews by Clarke et al.[19], Churchill et al.[18], and Strauss et al.[20] In the systematic reviews by Strauss et al.[20] and Jain et al.[16] it was unclear if literature selection and data extraction were conducted by two reviewers independently, and the list of excluded studies was not provided. Publication bias was not assessed and the quality of the included studies was not evaluated in Jain et al.[16]

The RCT by Kuyken et al.[21] was of good quality where allocation was concealed, research assessors were masked to treatment allocation for the duration of the follow-up period, and choice of sample size was justified. Allocation concealment was not described in the RCT by Meadows et al.[22]. The RCTs by Chiesa et al.[23] and Tovote et al.[26] had small sample sizes (23 and 31 patients in the mindfulness-based cognitive therapy treatment arms in RCTs by Chiesa et al.[23] and Tovote et al.[26], respectively). Assessors were not blinded in Tovote et al.[26]. It was not clear if allocation was concealed in the RCTs by Tovote et al.[26] and Bedard et al.[27]

Generalized anxiety disorder

In the systematic review by Bolognesi et al.[15] it was unclear if the literature selection and data extraction were conducted by two reviewers independently. Also, the list of excluded studies was not provided, publication bias was not assessed, the quality of the included studies was not evaluated, and non-RCTs were included. The inclusion of non-RCTs, which are of typically of lower methodological quality, could have greater risk of bias on the results, especially with interventions where blinding is not possible. In the RCTs by Hayes-Skelton et al.[29], it was not clear if assessors were blinded. In the RCT by Hoge et al.[30], it was not clear if allocation was concealed.

Substance use disorders
In the systematic review by Chiesa and Serretti[17], the literature selection and data extraction were conducted by two reviewers independently, the methodological quality were evaluated systematically, the list of excluded studies was provided, however risk of bias was not assessed and it included non-RCTs. In the RCT by Bowen et al.[28] it was not clear if allocation was concealed, and if assessors were blinded.

What are the evidence-based guidelines regarding the use of mindfulness interventions for the treatment of adults with PTSD, GAD, depression, or substance use disorders?

The guidelines by the Management of Post-Traumatic Stress working group,[34] NICE,[9] SIGN,[33] and the Management of Major Depressive Disorder Working Group[35] were developed by working groups of professionals from relevant clinical fields and expertise. These guidelines were based on systematic reviews of the literature, evidence synthesis and evaluation, and included clear processes of recommendation formulation. The guidelines were validated with different review processes. The reviewers did not identify relevant limitations for the four guidelines.

The CANMET guidelines by Parikh et al.[32] was based on a systematic review of the literature, and was validated though an internal and external review process. However, the authors did not report the composition of the working group and their backgrounds, and it was not clear if the quality of the included studies and evidence was critically appraised.

The New South Wales Department of Health guidelines was developed by a working group of allied health workers.[10] The authors of this guideline did not report the methods used to search and select literature and evidence. Further, the methods to evaluate the quality of evidence, formulate the recommendations, and validate the guidelines were not reported.[10]

Summary of Findings

A summary of individual study findings is presented in Appendix 4.

What is the clinical effectiveness of mindfulness interventions for the treatment of adults with PTSD, GAD, Depression, or substance use disorders?

Post-traumatic stress disorder
The RCT by Azad and Zadeh[24] reported that in comparison with the control group, there was a statistically significant increase in the mean scores of the QoL measures of the mindfulness-based stress reduction group in the post-test and delayed post-test in veterans with PTSD ($P < 0.01$, Table A7). The RCT by Omidi et al.[25] indicated that in veterans with PTSD, mindfulness-based stress reduction and treatment as usual showed that anger and vitality scales have no statistically significant differences, but on the other scales for depression, dizziness, fatigue and tension showed statistically significant differences between the two groups in favour of mindfulness based stress reduction ($P <0.01$, Table A7). The RCT by Kearney et al.[31] indicated that among veterans with PTSD, there was no statistically significant difference between mindfulness-based stress reduction and treatment as usual groups in PTSD and depression symptoms at the post treatment and 4-month time points. For the mental health-related QOL measure, there was a medium-to-large effect size in favour of mindfulness-based stress reduction at post treatment with a mean difference in the Mental Component Summary Score of the SF-8 (0.69, 95% CI: 0.07, 1.32, Table A7), but at 4 months there was no statistically

significant difference between treatment groups. For the physical health-related QOL measure, there was no statistically significant difference between treatment groups at post treatment but at 4 months there was a medium-to-large effect size in favour of mindfulness based stress reduction mean difference in the PCS Physical Component Summary of the SF-8 (0.73, 95% CI: 0.09, 1.37, Table A7).

Depression

The systematic review and meta-analysis by Clarke et al.[19] found that the average risk of developing a new episode of depression by 12 months was reduced by 21% for the mindfulness-based cognitive therapy group (relative risk = 0.79, 95% CI, 0.69 to 0.91, Table A7). The systematic review and meta-analysis by Strauss et al.[20] reported that there were significant post-intervention between-group differences for individuals diagnosed with a depressive disorder with a large effect size in favour of the MBI group (Hedges g = -0.73, 95% CI,-1.36 to -0.09, P = 0.03, Table A7). The systematic review by Churchill et al.[18] reported a statistically significant difference in depression levels, favouring acceptance and commitment therapy compared with treatment as usual with a mean difference of -0.60 (95% CI -1.16, -0.04, P = 0.035, Table A7). The systematic review by Jain et al.[16] reported that relative to the control group (waiting list or treatment as usual), the between-group effect sizes (Hedges g) favoured mindfulness-based cognitive therapy (Hedges g effect size, 0.47 to 1.09, Table A7). The authors reported that the between-group effect size favoured mindfulness-based cognitive therapy when compared to a psychoeducation control group (Hedges g effect size, 0.75, Table A7). There were no statistically significant differences between mindfulness-based cognitive therapy and cognitive behavior therapy in reduction of depressive symptoms among patients with major depression in two studies.[16]

Kuyken et al.[21] found that the time to relapse or recurrence of depression did not differ between mindfulness-based cognitive therapy with support to taper or discontinue antidepressant treatment and maintenance antidepressants over 24 months, nor did the number of serious adverse events. Also there was no statistically significant difference between treatment groups for depression symptoms and QoL. Meadows et al.[22] reported that the average number of days with major depression was 65 for mindfulness-based cognitive therapy participants, significantly less than those for controls (112 days). It was also reported that fewer mindfulness-based cognitive therapy participants relapsed in both year 1 (89 [33.7%] vs. 94 [46.8%]) and year 2 (89 [27.0%] vs. 89 [39.3%]) compared to controls. The Kaplan-Meier survival analysis for time to first depressive episode was non-significant, although trends favoring the mindfulness-based cognitive therapy group were suggested. Chiesa et al.[23] reported that both Hamilton Rating Scale for Depression and Beck Depression Inventory II (BDI-II) scores, as well as QoL showed higher improvements, which were particularly evident over the long-term period, in the mindfulness-based cognitive therapy group than in the psychoeducation group. Tovote et al.[26] found that participants receiving mindfulness-based cognitive therapy and cognitive behavior therapy reported significantly greater reductions in depressive symptoms compared with patients in the waiting list control condition. Both mindfulness-based cognitive therapy and cognitive behavior therapy also had significant positive effects on anxiety, and well-being. Bedard et al.[27] reported a greater reduction in BDI-II scores for the mindfulness-based cognitive therapy group than the control group. The improvement of BDI-II scores were maintained at the 3-month follow-up. On the other hand there was no statistical significance for either The Patient Health Questionnaire-9 or Symptom Checklist-90-Revised) depression scales.

Generalized anxiety disorder

The systematic review by Strauss et al.[20] included one study for patients with GAD indicating a statistically significant post-intervention between-group differences favoring MBI on primary symptom severity when compared with the inactive control group (mean difference [-5.29, 95% CI -6.87, -3.72]). The systematic review by Bolognesi et al.[15] reported that in one study, an 8-week group intervention based on mindfulness-based stress reduction significantly reduced anxiety and depressive symptoms, while another study reported a significant reduction in anxiety symptoms, but not in depressive symptoms among GAD patients treated with mindfulness-based stress reduction compared to an education program group. Another study found that eight weekly group classes of mindfulness-based stress reduction had sustained beneficial effects compared with a wait-list comparison group. It also indicated that in two open-label non-controlled studies, the efficacy of 8 weeks of mindfulness-based cognitive therapy significantly decreased anxiety, tension, worrying and depressive symptoms. In another study, the mindfulness-based cognitive therapy group demonstrated significantly greater decreases than the education program across all anxiety and depression scales. Another study reported that acceptance-based behavior therapy was associated with considerable improvements in anxiety, worrying and depression at the conclusion of treatment, with benefits persisting at 3 months follow-up. In two studies, acceptance-based behavior therapy was more effective in decreasing anxiety and depressive symptoms when compared to a waiting list.

Hayes-Skelton et al.[29] indicated that there was no statistically significant difference between acceptance-based behavior therapy and applied relaxation in clinician's severity rating, Structured Interview Guide for the Hamilton Anxiety Rating Scale (HAM-A), and Quality of Life Inventory scales, while Hoge et al.[30] reported that there was no significant difference between mindfulness-based stress reduction and stress management education groups in HAM-A scores. Mindfulness based stress reduction, was associated with a significantly greater reduction in anxiety as measured by the Clinical Global Impression of Severity, the Clinical Global Impression of Improvement, and the Beck Anxiety Inventory. Mindfulness-based stress reduction was also associated with greater reductions than stress management education in anxiety and distress ratings.

Substance use disorders

The systematic review by Chiesa and Serretti[17] indicated that mindfulness-based relapse prevention outperforms programs based on the 12-step program, and that dialectical behavioral therapy was significantly more effective than no-treatment conditions for the reduction of substance use and misuse in heterogeneous samples of drug users. Smoking cessation studies consistently document that different MBIs including acceptance and commitment therapy and mindfulness-based relapse prevention can be as or more effective than some established treatments for smoking cessation and that mindfulness-based stress reduction could have at least a non-specific effect on smoking cessation. Positive findings were likewise observed in participants with opiate dependence and in marijuana misusers. Lack of randomization details, objective measures of drug use and of information about treatment adherence, as well as small sample sizes raised concerns as to whether observed findings were actually due to the delivered interventions or are more properly attributable to methodological biases of included studies.

Bowen et al.[28] reported that compared with treatment as usual, participants assigned to mindfulness-based relapse prevention reported significantly lower risk of relapse to substance use and heavy drinking and, among those who used substances, significantly fewer days of substance use and heavy drinking at the 6-month follow-up. Relapse prevention showed an

advantage over mindfulness-based relapse prevention in time to first drug use. At the 12-month follow-up, mindfulness-based relapse prevention participants reported significantly fewer days of substance use and significantly decreased heavy drinking compared with relapse prevention and treatment as usual.

What are the evidence-based guidelines regarding the use of mindfulness interventions for the treatment of adults with PTSD, GAD, Depression, or substance use disorders?

Post-traumatic stress disorder
The Management of Post-Traumatic Stress working group suggested that mindfulness might be used as adjunctive therapy of hyperarousal symptoms of PTSD.[34] However, the authors reported that there was no evidence that mindfulness is more effective than standard stress inoculation techniques.

Depression
The guidelines by NICE,[9] SIGN,[33] CANMAT,[32] and the Management of Major Depressive Disorder Working Group[35] recommended that use of mindfulness in the maintenance phase for patients who have high risk of depression relapse.

Substance use disorders

The guideline by the New South Wales Department of Health suggested that mindfulness could be used to treat problematic drug and alcohol users.[10]

Limitations
There were no systematic reviews and only three RCTs identified for PTSD in this review; therefore, there is limited evidence available to address the research question regarding PTSD. All three RCTs had small sample size which limits the generalizability of the findings. All three RCTs used a mindfulness-based stress reduction intervention, hence there no evidence on other mindfulness interventions on PTSD. The study results were inconsistent in terms of statistical significance of the between-group difference. The evidence-based guidelines on PTSD lacked specific information regarding which behavioural interventions should be considered for PTSD. Due to the limited number of mindfulness studies identified and the poor quality of the clinical trials, it is difficult to draw definitive conclusions regarding the clinical effectiveness of mindfulness on PTSD.

Although numerous studies have been published on this topic, considerable heterogeneity was found in this review in terms of patient population and interventions studied. This is expected given that depression is broad term describing classes of common psychiatric disorders. Furthermore, these conditions may be associated with a range of comorbidities. Indeed, this review identified studies that have evaluated the effectiveness of mindfulness in patients with comorbidities. The majority of the literature on depression has been focused on mindfulness-based cognitive therapy, hence there is limited evidence on the impact of other mindfulness interventions on depression.

The literature search did not identify evidence-based guidelines regarding the use of mindfulness interventions for the treatment of adults with GAD. One systematic review and two RCTs were identified in this review for GAD. The methodological quality of the systematic review was low. Therefore, there is limited evidence available to address the research questions

regarding GAD. Each of the RCTs investigated a different mindfulness intervention with no replication of findings. Both RCTs had a small sample size.

One systematic review, one RCT, and one set of evidence-based guidelines were identified in this review for substance use disorders. The SR, RCT and the guideline were all of low methodological quality. The guideline recommendation was supported by at least Level 3 research and expert clinical opinion.

In all RCTs, methods for allocation concealment were not documented, and due to the nature of the intervention, patients participating in mindfulness interventions could not be blinded to treatment allocation arms.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Mindfulness is a form of complementary and alternative medicine with an emerging evidence base for the treatment of patients with mental health disorders including PTSD, GAD, depression and substance use disorders. The strongest evidence base exists for the use of mindfulness in treating depression. Two meta-analyses, two systematic reviews and five RCTs suggest that mindfulness may offer some benefit compared to treatment as usual or psycho-education, but may not offer additional benefits as an adjunct to pharmacological therapy when compared to pharmacological treatment alone. The type of mindfulness provided appeared to influence the effectiveness of the intervention. Conclusions based on this collective evidence base are limited due to the heterogeneity between studies and the highly selected patient populations.

The effectiveness of mindfulness in treating PTSD is unclear. Three RCTs found opposite effects in veterans with PTSD, where one RCT found that mindfulness training can improve the QoL of veterans with PTSD when compared with no treatment; another RCT found no significant differences in anger and vitality scales, but other scales such as depression, dizziness, fatigue and tension significantly favoured mindfulness when compared with treatment as usual. The third study found no significant difference between mindfulness and treatment as usual in PTSD and depression symptoms.

The effectiveness of mindfulness in treating GAD is unclear. While one systematic review concluded that mindfulness techniques may have beneficial effects in treating GAD, one included RCT reported no significant difference between acceptance-based behavioral therapy and applied relaxation in clinician's severity rating, anxiety and QoL scales. Another included RCT reported no significant difference between a mindfulness-based stress reduction program and a stress management education program in one of the anxiety measure, while there was significant difference between both groups in favour of mindfulness-based stress reduction in other anxiety measure.

The evidence for the efficacy of mindfulness as a treatment for individuals with substance use disorders was limited, where only one RCT was identified which concluded that the mindfulness intervention was more effective than treatment as usual in lowering risk of relapse to substance use and heavy drinking. The only systematic review for substance use disorders included in this report concluded a lack of randomization or of randomization details, objective measures of drug use, and of information for treatment adherence, as well as small sample sizes, and raised concerns as to whether observed findings were actually due to the delivered interventions or are more properly attributable to methodological biases of included studies.

Six evidence-based guidelines considered the use of mindfulness in clinical practice, of which one suggested that mindfulness may be considered for adjunctive treatment of hyperarousal symptoms in patients with PTSD, although there is no evidence that these are more effective than standard stress inoculation techniques. Four guidelines stated that mindfulness is recommended to reduce relapse in patients with depression, or during the continuation phase of treatment with patients at high risk for relapse, or as second-line therapy for maintenance phase of major depression. One guideline suggested that Mindfulness-Based Stress Reduction can be used to treat problematic drug and alcohol use problems by suitably trained and experienced drug and alcohol professionals. No guidelines were found for GAD.

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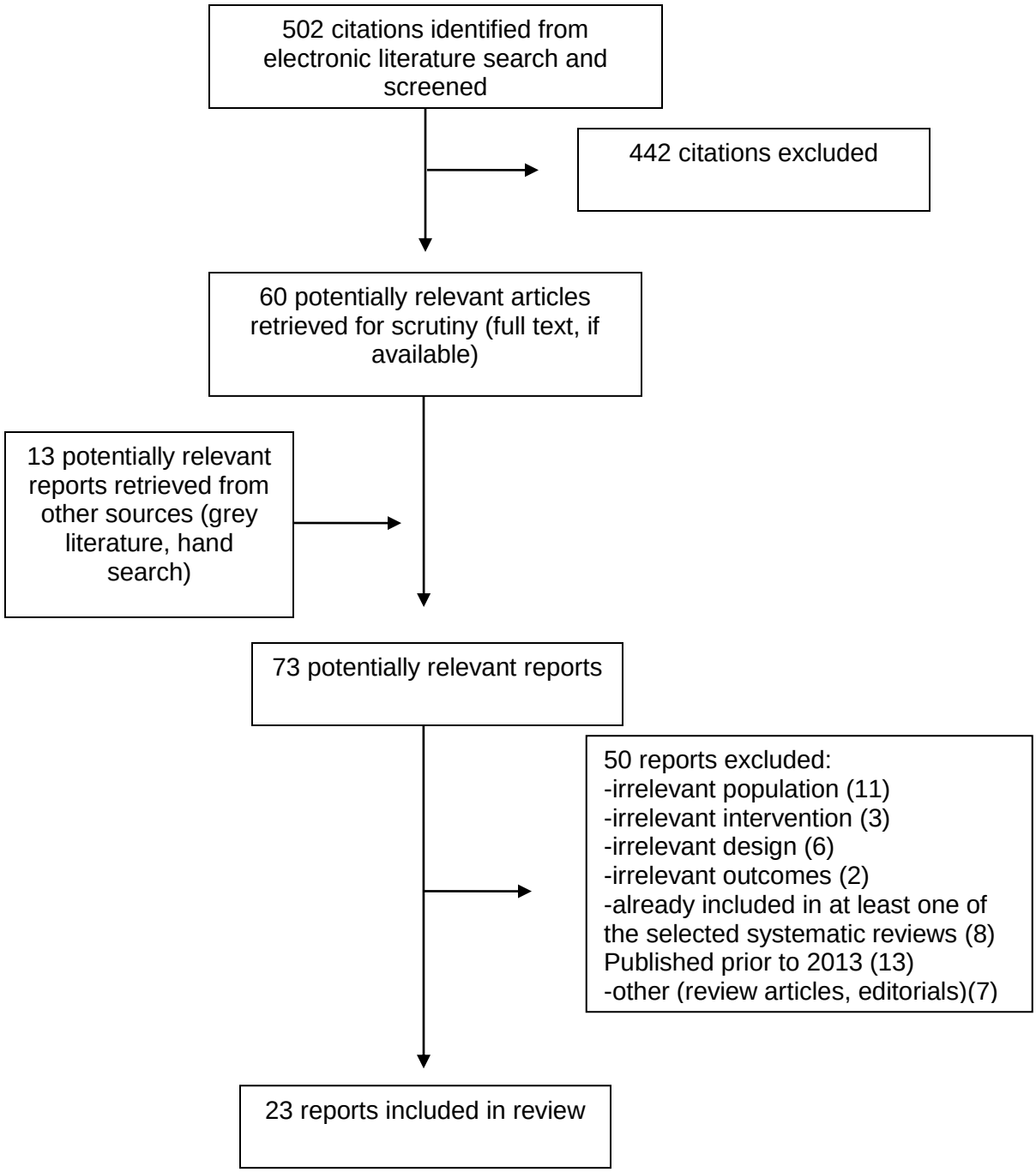
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Characteristics of Included Publications

Table A1: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country	Types and numbers of primary studies included	Population Characteristics	Intervention	Comparator(s)	Clinical Outcomes, Length of Follow-Up	Notes
Clarke et al. 2015,[19] UK	SR and MA, included RCT with minimum 1 year follow-up after randomization and with sample size ≥ 5 patients. Literature search: from inception to December 2013. 29 trials were included in the narrative review and 22 trials included in the meta-analysis. 7 of these trials used MBCT	Adults with full or partial remission from depression. Number of patients ranged from 60 to 274 in MBCT trials	Non-pharmacological intervention aimed at reducing relapse of depression. All 7 MBCT studies offered eight weekly two-hour sessions to groups of between 9 and 15 people with some variation in the number of additional sessions offered from none to monthly sessions for the trial duration	Any comparator. TAU was used in 4 out of the 7 MBCT studies, maintenance ADM was used in 1 MBCT study, ADM/clinical management + placebo was used in 1 study, and Cognitive psychological education + TAU or TAU was used in one study	Relapse of depression measured using DSM-IV diagnosis of MDE in two studies, DSM-IV diagnosis of MDE (SCID) in two studies, 16+ on the HRSD-17 assessed twice then criteria for MD measured with SCID in one study, DSM-III-R criteria for MDE (SCID) in one study and Criteria for MDE ≥ 2 weeks (SCID) in one study. Follow-up ranged from 52 to 86 weeks	
Jain et al. 2015,[16] US	SR included RCTs only. Literature search was through January 2014. 18 trials were included in the systematic review. 8 of these trials used MBCT	Adult patients suffering from depressive disorder (i.e. MD, dysthymia, or both) Number of patients ranged from 18 to 219 in MBCT trials	Meditation therapies	Not specified. TAU was used in 4 studies out of the 8 trials, PED was used in 1 trial, ADM was used in 1 study, wait list was used in 1 study, and CBT was used in 2 studies	Reduction of depressive symptoms using BDI-II in 3 studies, HRSD in 3 studies, BDI in one study, and general severity index of brief symptom inventory in one study. Length of follow-up was not mentioned	The review included two trials using MBCT that are common with other systematic reviews

Table A1: Characteristics of Included Systematic Reviews and Meta-Analyses						
First Author, Publication Year, Country	**Types and numbers of primary studies included**	**Population Characteristics**	**Intervention**	**Comparator(s)**	**Clinical Outcomes, Length of Follow-Up**	**Notes**
Churchill et al. 2013,[18] UK	SR included RCTs only. Literature search was through March 2013. 4 trials were included in the review. 1 of these trials used ACT	Adult patients with acute depression. Number of patients included in ACT trial was 54	ACT, compassionate mind training, functional analytic psychotherapy, dialectical behavior therapy, MBCT, extended behavioral activation and metacognitive therapy. The study that used ACT intervention offered 4 weekly sessions in a group format of 2 to 10 participants	Treatment as usual, waiting list, attention placebo, psychological placebo. Supportive group comparison was used as comparator in the study that used ACT intervention	Number of participants who responded to treatment and number of participants who remitted. The trial with ACT intervention used BDI-II to measure continues change in depression scores	
Strauss et al. 2014,[20] UK	SR and MA of RCTs. Literature search was through July 2013. 12 trials were included in this review, of those six trials used MBCT, 5 used MBSR, and one used PBCT intervention	Adult patients with anxiety or depressive disorder. 4 trials included patients with depression (three of these trials used MBCT, and one trial used PBCT, with number of patients ranged from 18 to 69), and one trial included 31	MBIs	Group CBT, group psychoeducation and inactive control conditions (TAU, wait list, aerobic exercise). In the Depression studies group psychoeducation was used in 1 study, group CBT was used in 1 study and TAU was used in two studies	BDI-II, and HRSD	The review included two trials on depression patients that are common with other systematic reviews

Table A1: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country	Types and numbers of primary studies included	Population Characteristics	Intervention	Comparator(s)	Clinical Outcomes, Length of Follow-Up	Notes
		patients with GAD where MBSR was used				
Bolognesi et al. 2014,[15] UK	SR Literature search was through September 2012. 3 studies using MBCT, 3 studies using MBSR and three studies using ABBT were included in this review	Patients with GAD. Number of patients ranged from 11 to 46 in MBCT trials, from 18 to 76 in MBSR trials, and 16 to 31 in ABBT trials	CBT, CBT Packages, new CBT approaches, third wave CBT, Internet computer based CBT, psychodynamic therapy, brief psychodynamic therapy, AR and mindfulness	Any or none No control group was used in two of the MBCT studies, and ADE was used in 1 study. Waiting list was used in 1 study, no control group was used in 1 study, and education program was used in 1 study in the MBSR studies. Waiting list was used in two of the ABBT studies, and no control group used in 1 study	BAI HAM-A HRSD PSWQ	
Chiesa and Serretti 2014,[17] Italy	SR Literature search was through December 2011. 24 studies were included of which 14 were RCTs and ten	adult patients receiving treatment for SUM 12 studies focused on alcohol and/or heterogeneous	MBI eight studies focused on MBSR or related MBI, five on ACT, three on 3S-therapy, two on DBT, one study focused on a Vipassana retreat,	either inactive (e.g., waitlist) or active (i.e., condition intended to control for non-specific effects of MBIs 10 compared MBIs to a waitlist, eight	difference between MBIs and active or inactive comparators on measures of objective and subjective SUM reduction	

Table A1: Characteristics of Included Systematic Reviews and Meta-Analyses						
First Author, Publication Year, Country	**Types and numbers of primary studies included**	**Population Characteristics**	**Intervention**	**Comparator(s)**	**Clinical Outcomes, Length of Follow-Up**	**Notes**
	were non-RCTs	substance use, four on cigarette smoking, three on opiate use, one on marijuana use, and one on metamphetamine use	one study focused on a goal management training in adjunct to mindfulness meditation, and one study focused on a brief motivational intervention in adjunct to mindfulness meditation	compared MBIs with an active treatment, two compared MBIs with non-specific educational interventions designed to be structurally equivalent to the MBIs		

3S-therapy = Spiritual self-schema therapy; ABBT = Acceptance-based behavior therapy; ACT = Acceptance and Commitment Therapy; ADE = anxiety disorder education program; ADM = antidepressant medication; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory II; DSM = Diagnostic Statistical Manual; CBT = cognitive behavior therapy; GAD = Generalized Anxiety Disorder; DBT = Dialectical behavioral therapy; HAM-A = Hamilton Anxiety Rating Scale; HRSD = Hamilton Rating Scale for Depression; MA = meta-analysis; MBCT = Mindfulness-Based Cognitive Therapy; MBI = Mindfulness-based intervention; MBSR = Mindfulness-Based Stress Reduction; MD = major depression; MDE = Major Depressive Episode; PBCT = Person-Based Cognitive Therapy; PED = psychoeducation group; PSWQ = Penn State Worry Questionnaire; RCT = randomized controlled trial; SCID = Structured Clinical Interview for DSM Disorders; SR = systematic review; SUM = substance use and misuse; TAU = treatment as usual

Table A2: Characteristics of Included Clinical Studies					
First Author, Publication Year, Country, Study Name	**Study Design**	**Patient Characteristics**	**Intervention(s)**	**Comparator(s)**	**Clinical Outcomes**
Patients with Post-Traumatic stress disorder (PTSD) Trials					
Azad and Zadeh 2014,[24] Iran	RCT and included a pre-test, post-test and delayed post-test with a control group. Single-blind Single center N=32	Male warfare veterans of Iran-Iraq war diagnosed with PTSD	MBSR, n=14	No treatment, n=14	WHOQOL-26
Omidi et al. 2013,[25] Iran	RCT Single center N=62	Veterans with PTSD	MBSR, n=31	TAU, n=31	BRUMS
Kearney et al. 2013,[31] US	RCT Single center N = 47	veterans with PTSD	MBSR, n=25	TAU, n=22	PTSD checklist civilian version, Life events checklist The patient Health Questionnnaire-9 The Short Form-8
Patients with depression					
Kuyken et al. 2015,[21] UK, PREVENT study	RCT Single-blind multicenter N=424	Adult patients with diagnosis of recurrent MD in full or partial remission, with three or more previous MDEs and on a therapeutic dose of maintenance antidepressant drugs	8-week MBCT class that included support to taper or discontinue maintenance antidepressant medication (MBCT-TS), n=212	maintenance antidepressant treatment, n=212	Time to relapse or recurrence of depression. number of depression free days, QoL
Meadows et al. 2014,[22] Australia	RCT Single-blind Multicenter N=203	Non-depressed adults with a history of three or more episodes of depression	MBCT + DRAM, n=101	DRAM, n=102	proportion of relapse/recurrence days in MDEs time to relapse/recurrence

Table A2: Characteristics of Included Clinical Studies					
First Author, Publication Year, Country, Study Name	**Study Design**	**Patient Characteristics**	**Intervention(s)**	**Comparator(s)**	**Clinical Outcomes**
Chiesa et al. 2015,[23] Italy	RCT N=43	Patients diagnosed with MD, single or recurrent episode, age between 18 and 65 years, on treatment with antidepressants at adequate dosages for at least 8 weeks before study beginning and failure to achieve remission during the screening visit	MBCT, n=23	Psychoeducation, n=20	HRSD BDI-II BAI PGWBI
Tovote et al. 2014,[26] Netherlands	RCT Single-blind Multicenter N=94	Patients aged between 18 and 70 years with type 1 or 2 diabetes diagnosed at least 3 months prior to inclusion and having symptoms of depression as indicated by BDI-II score of ≥ 14	MBCT, n=31	CBT, n=32, waiting list, n=31	BDI-II HAMD-7
Bedard et al. 2014,[27] Canada	RCT Multicenter N=105	adults with symptoms of depression after a traumatic brain injury	MBCT, n=57	Waiting list, n=48	BDI-II PHQ-9 SCL-90-R
Patients with generalized anxiety disorder					
Hayes-Skelton et al. 2013,[29] US	RCT N=81	Adult patients with principal diagnosis of GAD with at least moderate severity were included	ABBT, n=40	AR, n=41	CSR SIGH-A QOLI

Table A2: Characteristics of Included Clinical Studies

First Author, Publication Year, Country, Study Name	Study Design	Patient Characteristics	Intervention(s)	Comparator(s)	Clinical Outcomes
Hoge et al. 2013,[30] US	RCT Single-blind Single center N=93	Adult patients who met DSM-IV criteria for current primary GAD and designated GAD as the primary problem, and scored 20 or above on the HAM-A	MBSR, n=48	SME, n=41	HAMA-A CGI-S CGI-I BAI
Patients with substance use disorders					
Bowen et al. 2014,[28] US	RCT Multicenter N=286	Adult patients enrolled in a substance abuse aftercare program	MBRP, n=103	RP, n=88 or TAU, n=95	relapse to drug use and heavy drinking frequency of substance use in the past 90 days

ABBT = Acceptance-Based Behavioral Therapy; ADIS-IV = Anxiety Disorders Interview Schedule; AR = Applied Relaxation; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory II; BRUMS = Inventory of mood status; CBT = cognitive behavior therapy; CGI-S = Clinical Global Impression of Severity; CGI-I = Clinical Global Impression of Improvement; CSR = clinician's severity rating; DRAM = Depression Relapse Active Monitoring; HAM-A = Hamilton Anxiety Rating Scale; HAMD-7 = 7 Item Hamilton Depression Rating Scale; HRSD = Hamilton Rating Scale for Depression; MBCT = Mindfulness-Based Cognitive Therapy; MBCT-TS = MBCT with support to taper or discontinue antidepressant treatment; MBRP = Mindfulness-based relapse prevention; MBSR = Mindfulness-Based Stress Reduction; MD = major depression; MDE = major depressive episodes; PGWBI = Psychological General Well Being Index; PHQ-9 = The Patient Health Questionnaire-9; PTSD = post-traumatic stress disorder; QoL = Quality of Life; QOLI = Quality of Life Inventory; RCT = randomized controlled trial; RP = relapse prevention; SCL-90-R = Symptom Checklist-90-Revised; SIGH-A = Structured Interview Guide for the Hamilton Anxiety Rating Scale; SME = Stress Management Education; TAU = treatment as usual; WHOQOL-26 = World Health Organization Quality of Life Questionnaire

Table A3: Characteristics of Included Guidelines				
Objectives			**Methodology**	
Intended users/ Target population	**Intervention and Practice Considered**	**Major Outcomes Considered**	**Evidence identification, Synthesis and evaluation**	**Recommendations development and Evaluation, and guideline validation**
Post-traumatic stress disorder				
The Management of Post-Traumatic Stress Working Group, 2010[34] – US Department of Veterans Affairs				
The intended users included nurses and advanced practice nurses, health care providers, health plans, hospitals, managed care organizations, physicians and their assistants, psychologists/non-physician behavioral health clinicians, public health departments, social workers and substance use disorders treatment provides. The target population includes adult patients with PTSD treated in by the Veterans Administration or Department of Defense	• PTSD screening • Management of acute stress reaction • Management of PTSD • Treatment interventions for PTSD ○ Selection of therapy ○ Psychotherapy ○ Pharmacotherapy ○ Adjunctive services ○ Somatic treatment ○ Complementary & alternative medicine ▪ mindfulness ▪ yoga ▪ acupuncture ▪ massage	• Improvement in QoL • Reduced morbidity/mortality • Improvement over long term • Patient satisfaction • Co-morbidity • Improvement of symptoms	A working group composed from different clinical fields and methodologists (data analysts) participated in the screening, selection, data extraction, and evidence evaluation from the selected literature. Evidence synthesis was based on review of published meta-analyses and systematic review with evidence tables Quality and strength of evidence were evaluated by expert consensus, and they were rated according to a pre-defined scheme	Recommendations were formulated by a consensus among the participating clinical experts. The clinical experts used the synthesized evidence, and the strength of recommendations was based on the quality and strength of evidence. The guideline was validated by an external and internal reviews
Depression				
National Institute for Health & Clinical Excellence (NICE), 2010[9]				
The intended users were not explicitly specified. The target population is adults with	• psychological and psychosocial • cognitive behavioral therapies • mindfulness-based cognitive therapy	• mortality • morbidity • treatment complications • rates of relapse • late morbidity and	A systematic review of the literature was used to identify relevant evidence. Evidence was synthetized by meta-analyses and evidence profile tables. The quality of the included studies was	Recommendations were formulated by consensus among the working group after reviewing the evidence and its strength profile.

Table A3: Characteristics of Included Guidelines

Objectives			Methodology	
Intended users/ Target population	**Intervention and Practice Considered**	**Major Outcomes Considered**	**Evidence identification, Synthesis and evaluation**	**Recommendations development and Evaluation, and guideline validation**
depression	• behavioral activation • guided self-help • physical activity programs • interpersonal therapy • others	readmission • return to work • physical and social functioning • QoL • general health status • costs	evaluated before considering them as evidence	Validation of the guideline was done by the review of registered stakeholders who included patients, patients groups, and professional providing care for patients
Scottish Intercollegiate Guidelines Network (SIGN), 2010[33]				
The intended users included developers of mental health services, healthcare professionals in primary and secondary care. The target population included adult patients with depression and their carers	• Self-help • Structured exercise • Psychological therapies ○ Behavioral activation ○ CBT ○ Hypnotherapy ○ Mindfulness based cognitive therapy ○ Others	The primary outcome was reduction in depressive symptom. Secondary outcomes included illness duration, relapse, QoL and patient satisfaction	A systematic literature review was carried out. A working group of different clinical fields and methodologists participated in the development of the guideline. The selection and synthesis of each included study was done by two reviewers. The quality of the included studies was evaluated before considering them as evidence	Recommendations were formulated by expert consensus. Validation of the guideline was done through national open meeting and specialist review
Parikh et al., 2009[32] – Canadian Network for Mood and Anxiety Treatments (CANMAT)				
The intended users were not explicitly specified in the guideline. The target population was adults with MD	• Psychotherapy • CBT • Interpersonal therapy • MBCT • Psychodynamic psychotherapy • Cognitive Behavioural Analysis System of Psychotherapy • Behavioural Activation • Others	Outcomes were not explicitly reported in the guideline	A working group participated in the screening, selection, data extraction, and evidence evaluation from the selected literature. Evidence synthesis was based on review of published RCTs and meta-analyses and review with evidence tables. Quality of the included studies was not evaluated	The guideline provided high level evaluation of the strength of recommendations based on the type and number of studies supporting each recommendation. The guideline was validated by an external and internal reviews

Table A3: Characteristics of Included Guidelines

Objectives			Methodology	
Intended users/ Target population	**Intervention and Practice Considered**	**Major Outcomes Considered**	**Evidence identification, Synthesis and evaluation**	**Recommendations development and Evaluation, and guideline validation**
The Management of MD Working Group, 2008[35] - US Department of Veterans Affairs				
The intended users included all healthcare professionals who have direct contact with patients with MD, and who make decisions about their care. The target population was adult patients with MD	• Pharmacotherapy • Psychotherapy ○ CBT ○ Interpersonal psychotherapy ○ Problem solving therapy ○ Behavioral activation ○ Acceptance and mindfulness ○ Others	• depressive symptoms • functional status • suicide risk • adverse effects and tolerability • adherence to treatment	A working group composed from different clinical fields and methodologists (data analysts) participated in the screening, selection, data extraction, and evidence evaluation from the selected literature. Evidence synthesis was based on review of published meta-analyses and systematic review with evidence tables. Quality and strength of evidence were evaluated by expert consensus, and they were rated according a predefined scheme	Recommendations were formulated by a consensus among the participating clinical experts. The clinical experts used the synthesized evidence, and the strength of recommendations was based on the quality and strength of evidence. The guideline was validated by an external and internal reviews
Substance use disorders				
Mental Health and Drug and Alcohol Office, 2008[10] – New South Wales Department of Health				
The intended users included all allied health disciplines within drug and alcohol specialist services that provide direct clinical psychosocial interventions	• Cognitive Behavioural Therapies • Psychodynamic and interpersonal approaches • Emotion Regulation • Mindfulness-Based Stress Reduction • Dialectical Behaviour Therapy • Acceptance and Commitment Therapy • Family approaches • Others	The guideline did not specify outcomes, but several co-morbidities were evaluated. These included depression, anxiety, psychosis, personal disorders, trauma, anger/aggression, pain and blood-borne viruses	The process of evidence collection and synthesis was not reported in the guideline. The authors of the guideline provided an evaluation for the strength of evidence-based on the type and number of studies, but the quality of the included studies was not evaluated or reported	The method used to formulate the recommendations was not reported. The method of validation was not reported

CBT = cognitive behavior therapy; MD = major depression; PTSD = post-traumatic stress disorder; QoL = Quality of Life

APPENDIX 3: Critical Appraisal of Included Publications

Table A4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[12]

Strengths	Limitations
Clarke et al. 2015,[19] UK, SR and MA.	
• comprehensive literature search based on pre-defined criteria • literature selection and data extraction were conducted by two reviewers independently • risk of bias for included studies, and the quality of the evidence available were assessed • results of the quality assessment were considered when formulating conclusions • conflict of interest was stated	• List of excluded studies was not provided
Jain et al. 2015,[16] US, SR	
• Comprehensive literature search based on pre-defined criteria	• Unclear if literature selection and data extraction were conducted by two reviewers independently • Conflict of interest was not stated • No list of excluded studies was provided • Publication bias was not assessed • The quality of the included studies was not evaluated
Churchill et al. 2013,[18] UK, SR	
• comprehensive literature search based on pre-defined criteria • literature selection and data extraction were conducted by two reviewers independently • list of excluded studies was provided • the methodological quality were evaluated systematically • risk of bias of individual studies was assessed • publication bias was assessed	• No limitations were identified
Strauss et al. 2014,[20] UK, SR and MA.	
• Comprehensive literature search based on pre-defined criteria • The methodological quality were evaluated systematically • Risk of bias of individual studies was assessed • Publication bias was assessed • Results of the quality assessment were considered when formulating conclusions	• Unclear if literature selection and data extraction were conducted by two reviewers independently • List of excluded studies was not provided • Conflict of interest was not stated
Bolognesi et al. 2014,[15] UK, SR	
• Comprehensive literature search based on pre-defined criteria	• Unclear if literature selection and data extraction were conducted by two reviewers independently • List of excluded studies was not provided • Conflict of interest was not stated • Publication bias was not assessed • The quality of the included studies was not evaluated • Included non-RCTs
Chiesa and Serretti 2014,[17] Italy	
• comprehensive literature search based on pre-defined criteria • literature selection and data extraction were conducted by two reviewers independently	• Risk of bias was not assessed • Included non-RCTs

• the methodological quality were evaluated systematically • list of excluded studies was provided • conflict of interest was stated • results of the quality assessment were considered when formulating conclusions	

Table A5: Strengths and Limitations of Randomized Controlled Trials using Downs and Black[13]

Strengths	Limitations
Patients with Post-Traumatic stress disorder (PTSD)	
Azad and zadeh 2014,[24] Iran	
• Objectives and inclusion/ exclusion criteria were stated • Patient characteristics, interventions, and outcomes were described • P-values provided	• it is not clear if the study was single blinded or not blinded at all • randomization method and allocation concealment were not described • the article did not precise if the analysis was based on the intention to treat or per-protocol dataset • small sample size
Omidi et al. 2013,[25] Iran	
• Objectives and inclusion/ exclusion criteria were stated • Patient characteristics, interventions, and outcomes were described • P-values provided	• randomization method was not described • patients and investigators were not masked to treatment allocation • allocation was not described • small sample size
Kearney et al. 2013,[31] US	
• Objectives and inclusion/ exclusion criteria were stated • Patient characteristics, interventions, and outcomes were described • Allocation was concealed, but the method used not described • P-values provided	• randomization method was not described • patients and investigators were not masked to treatment allocation • small sample size
Patients with depression	
Kuyken et al. 2015,[21] UK, PREVENT study	
• objectives and inclusion/ exclusion criteria were stated • patient characteristics, interventions, and outcomes were described • allocation was concealed • research assessors were masked to treatment allocation for the duration of the follow-up period • choice of sample size was justified • p-values provided • intent-to-treat analysis was used	• No limitations were identified
Meadows et al. 2014,[22] Australia	
• objectives and inclusion/ exclusion criteria were stated • single-blind • patient characteristics, interventions, and outcomes were described • choice of sample size was justified • p-values provided • intent-to-treat analysis was used	• It is not described how allocation was concealed
Chiesa et al. 2015,[23] Italy	
• objectives and inclusion/ exclusion criteria were stated	• small sample size

• single-blind • patient characteristics, interventions, and outcomes were described • allocation was concealed • p-values provided • intent-to-treat analysis was used	
Tovote et al. 2014,[26] Netherlands	
• Objectives and inclusion/ exclusion criteria were stated. • Patient characteristics, interventions, and outcomes were described. • P-values provided. • Intent-to-treat analysis was used.	• Small sample size. • Assessors were not blinded. • It is not clear if allocation was concealed.
Bedard et al. 2014,[27] Canada	
• Objectives and inclusion/ exclusion criteria were stated • Patient characteristics, interventions, and outcomes were described • Choice of sample size was justified • Research assistants collecting information were blind to group allocation • P-values provided	• It is not clear if allocation was concealed.
Patients with generalized anxiety disorder	
Hayes-Skelton et al. 2013,[29] US	
• Objectives and inclusion/ exclusion criteria were stated. • Patient characteristics, interventions, and outcomes were described. • Allocation was concealed. • P-values provided.	• It is not clear if assessor were blinded
Hoge et al. 2013,[30] US	
• Objectives and inclusion/ exclusion criteria were stated. • Patient characteristics, interventions, and outcomes were described. • Independent evaluators were blinded. • P-values provided.	• It is not clear if allocation was concealed.
Patients with substance use disorders	
Bowen et al. 2014,[28] US	
• Objectives and inclusion/ exclusion criteria were stated • Patient characteristics, interventions, and outcomes were described	• It is not clear if allocation was concealed. • Assessors were not blinded.

Table A6: Strengths and Limitations of Guidelines using AGREE II[14]

Strengths	Limitations
Post-traumatic stress disorder	
The Management of Post-Traumatic Stress Working Group, 2010[34] – US Department of Veterans Affairs	
• The guideline was developed by a working group of primary care givers, psychiatrists, psychologists, internal medicine physicians, pharmacologist, nurses, social workers and research analysts. • The working group had common orientation and training about the objectives and methods of the guidelines. • A systematic literature search was conducted and the working group participated in the screening, selection, data extraction, and quality evaluation of the included studies.	• No limitations were identified

• The recommendations were formulated by clinicians. The recommendation strength and the net benefit of interventions were based on quality and strength of evidence.	
Depression	
National Institute for Health & Clinical Excellence (NICE), 2010[9]	
• A working group composed of healthcare professionals, lay representatives and technical experts participated in the development of the guideline update • A systematic review of literature was used to identify relevant evidence • The quality of included evidence was evaluated • Recommendations were based on the trade-off between the benefits and downsides of treatment, economic considerations, and the values of the working group and society	• No limitations were identified
SIGN, 2010[33]	
• The guidelines were developed by a working group composed of relevant clinical field and expertise • A systematic review of literature was used to identify relevant evidence • The quality of included evidence was evaluated and weighted according to a rating scheme • The recommendations were based on expert consensus • The strength of recommendations was based on several factors that included the balance of benefit and harms, patient's values and preferences, and cost-effectiveness of the intervention.	• No limitations were identified
Parikh et al., 2009[32] – Canadian Network for Mood and Anxiety Treatments (CANMAT)	
• The guidelines were based on systematic review of the literature • The guidelines were validated by an external and internal review process	• The intended users and outcomes were not explicitly specified • The composition of the working group was not reported • The quality of the included studies was not evaluated
The Management of MD Working Group, 2008[35] - US Department of Veterans Affairs	
• The guidelines were developed by a working group of primary care givers, psychiatrists, psychologists, internal medicine physicians, pharmacologist, nurses, social workers and research analysts. • The working group had common orientation and training about the objectives and methods of the guidelines. • A systematic literature search was conducted and the working group participated in the screening, selection, data extraction, and quality evaluation of the included studies. • The recommendations were formulated by clinicians. The recommendation strength and the net benefit of interventions were based on quality and strength of evidence.	• No limitations were identified
Substance use disorders	
Mental Health and Drug and Alcohol Office, 2008[10] – New South Wales Department of Health	
• The guideline was developed by a working group of allied health workers.	• The methods used to search and select the literature was not reported • The quality of the included studies was not evaluated/reported • Method used to formulate the recommendations was not reported • The method of guideline validation was not reported

APPENDIX 4: Main Study Findings and Author's Conclusions

Table A7: Summary of Findings of Included Studies

Main Study Findings	Author's Conclusions
Patients with Post-Traumatic stress disorder (PTSD)	
Azad and Zadeh 2014,[24] Iran	
In comparison with the control group, there was a statistically significant increase in the mean scores of the physical and psychiatric health, social relationship and social setting and condition of the MBSR group in the post-test and delayed post-test ($P < 0.01$)	Mindfulness training can improve the QoL of veterans with PTSD
Omidi et al. 2013,[25] Iran	
Comparison of the results between the MBSR and TAU showed that anger and vitality scales have no significant differences, but on the other scales depression, dizziness, fatigue and tension showed significance difference between the two groups in favour of MBSR ($P < 0.01$)	MBSR is a useful method to regulate the mood state in veterans with PTSD who have difficulties in mood and emotions
Kearney et al. 2013,[31] US	
There was no significant difference between MBSR and TAU groups in PTSD and depression symptoms at the post treatment and 4-month time points. For mental HRQoL there was a medium-to-large effect size in favour of MBSR at post treatment (mean difference in the Mental Component Summary Score of SF-8 was 0.69, 95% CI: 0.07, 1.32), but at 4 months there was no significantdifference between treatment groups. For physical HRQoL there was no significance difference between treatment groups at post treatment but at 4 months there was a medium-to-large effect size in favour of MBSR (mean difference in the PCS Physical Component Summary of SF-8 was 0.73, 95% CI: 0.09, 1.37)	Additional studies are needed to assess MBSR for veterans with PTSD
Patients with Depression	
Clarke et al. 2015,[19] UK, SR and MA.	
The average risk of developing a new episode of depression by 12 months was reduced by 21% for MBCT (RR = 0.79, 95% CI, 0.69 to 0.91, $I^2 = 0\%$)	There was evidence that MBCT is effective in reducingrisk of relapse following recovery from depression. It was largely tested following medication, so its efficacy following psychological interventions is less clear
Jain et al. 2015,[16] US, SR	
Relative to wait list or treatment as usual controls, the between- group effect sizes (Hedges g) in the five studies using MBCT favour MBCT and were moderate to large (0.47 to 1.09). In the study that used psychoeducation control group arm, between- group effect size (Hedges g) favoured MBCT and was 0.75. Two studies for MD compared MBCT vs CBT and showed no significant differences in reduction of depressive symptoms between these two interventions	The role of meditation techniques in the clinical armamentarium for depression has not been firmly established. Existing RCTs are demonstrating reductions in depressive symptoms, and although the variability both within the clinical populations and the techniques studied suggests wide generalizability across depressive condition type and illness stage, the absence of well-matched control groups and the lack of large replication trials also limit the reliability and specificity of the results and conclusions that may be drawn
Churchill et al. 2013,[18] UK, SR	
A significant difference in depression levels favoured ACT compared with TAU, mean difference (-0.60, 95% CI -1.16, -0.04, P = 0.035)	While the findings from the review appear to suggest that third wave CBT approaches are more effective than TAU conditions in treating the acute symptoms of depression, the very low quality of the evidence

Table A7: Summary of Findings of Included Studies	
Main Study Findings	**Author's Conclusions**
	base limits the ability to draw conclusions on their efficacy, either as individual approaches or as a collective approach
Strauss et al. 2014,[20] UK, SR and MA.	
There were significant post-intervention between-group differences for people diagnosed with a depressive disorder with a large effect size in favour of MBI on primary symptom severity (Hedges g =-0.73, 95% CI,-1.36 to -0.09, z(3)= 2.24, P = 0.03)	Significant benefits relative to control conditions for primary symptom severity for people experiencing a current episode of depression following MBIs (namely MBCT or PBCT) were found
Kuyken et al. 2015,[21] UK, PREVENT study, RCT	
The time to relapse or recurrence of depression did not differ between MBCT-TS and maintenance antidepressants over 24 months, nor did the number of serious adverse events. Also there was no significant difference between treatment groups for depression symptoms and QoL	No evidence was found to conclude that MBCT-TS is superior to maintenance antidepressant treatment for the prevention of depressive relapse in individuals at risk for depressive relapse or recurrence. Both treatments were associated with enduring positive outcomes in terms of relapse or recurrence, residual depressive symptoms, and QoL
Meadows et al. 2014,[22] Australia, RCT	
The average number of days with major depression was 65 for MBCT participants significantly less than those for controls (112 days) Fewer MBCT participants relapsed in both year 1 (33.7% vs 46.8%) and year 2 (27.0% vs. 39.3%) compared to controls Kaplan-Meier survival analysis for time to first depressive episode was non-significant, although trends favoring the MBCT group were suggested	This study supports the effectiveness of MBCT in something closer to implementation in routine practice than has been studied hitherto. Observed effects were less strong than in some previous efficacy studies but appreciable and significant differences in outcome were detected. MBCT is most clearly demonstrated as effective for people receiving specialist care and seems to work well combined with antidepressants
Chiesa et al. 2015,[23] Italy, RCT	
Both HRSD and BDI scores, as well as QoL showed higher improvements, which were particularly evident over the long-term period, in the MBCT group than in the psychoeducation group	Results suggest the superiority of MBCT over psychoeducation for non-remitted MD subjects
Tovote et al. 2014,[26] Netherlands, RCT	
Participants receiving MBCT and CBT reported significantly greater reductions in depressive symptoms compared with patients in the waiting list control condition. Both interventions MBCT and CBT also had significant positive effects on anxiety, well-being	MBCT and CBT are effective in improving a range of psychological symptoms in individuals with type 1 and type 2 diabetes
Bedard et al. 2014,[27] Canada, RCT	
A greater reduction in BDI-II scores for the MBCT group than the control group. The improvement BDI-II scores was maintained at the 3-month follow-up. However there was no statistical significance for either PHQ-9 or SCL-90-R depression scales	Results are consistent with those of other researchers that use MBCT to reduce symptoms of depression
Patients with GAD	
Strauss et al. 2014,[20] UK, SR and MA.	
In the one study for patients with GAD, there were significant post-intervention between-group differences for people diagnosed with GAD with a large effect size in favour of MBI on primary symptom severity (Hedges g =-5.29, 95% CI, -6.87 to -3.72)	No conclusion was mentioned related to GAD
Bolognesi et al. 2014,[15] UK, SR	
MBSR: One study reported that an 8-week group intervention based on MBSR significantly reduced anxiety and depressive symptoms in individuals with GAD, another study reported a significant reduction in anxiety symptoms,	mindfulness techniques have shown beneficial effects in treating GAD

Table A7: Summary of Findings of Included Studies	
Main Study Findings	**Author's Conclusions**
but not in depressive symptoms, in GAD patients treated with MBSR compared to an education program group. Another study found that in patients with GAD, MBSR had sustained beneficial effects compared to a waiting list control condition. MBCT: two open non-controlled studies suggested the efficacy of MBCT significantly decreased anxiety, tension, worrying and depressive symptoms in patients with GAD. In another study the MBCT group demonstrated significantly greater decreases than the education program across all anxiety and depression scales in patients with GAD ABBT: A study in GAD suggested that ABBT was associated with considerable improvements in anxiety, worrying and depression at the conclusion of treatment, with benefits persisting at 3 months follow-up In two studies that compared to waiting list, it was found that ABBT more effective in decreasing anxiety and depressive symptoms in patients with GAD	
Hayes-Skelton et al. 2013,[29] USA, RCT	
There was no significant difference between ABBT and AR in CSR, SIGH-A, and QOLI scales	ABBT is a viable alternative for treating GAD
Hoge et al. 2013,[30] US, RCT	
There was no significant difference between MBSR and SME groups in HAM-A scores at endpoint. MBSR, was associated with a significantly greater reduction in anxiety as measured by the CGI-S, the CGI-I, and the BAI. MBSR was also associated with greater reductions than SME in anxiety and distress ratings	Results suggest that MBSR may have a beneficial effect on anxiety symptoms in GAD, and may also improve stress reactivity
Patients with Substance Use Disorders	
Chiesa and Serretti 2014,[17] Italy, SR	
MBRP outperforms programs based on the 12-step program, Vipassana retreat outperformed an educational Intervention and that both DBT and 3S-therapy were significantly more effective than no-treatment conditions for the reduction of SUM in heterogeneous samples of drug users. Smoking cessation studies consistently document that different MBIs including ACT and MBRP can be as or more effective than some established treatments for smoking cessation (i.e., NRT and CBT) and that MBSR could have at least a non-specific effect on smoking cessation. Positive findings were likewise observed in participants with opiate dependence and in marijuana misusers. Lack of randomization or of randomization details, small sample size, lack of objective measures of drug use and of information about treatment adherence raise concerns as to whether observed findings are actually due to the delivered interventions or are more properly attributable to methodological biases of included studies	Current evidence suggests that MBIs can reduce the consumption of several substances of misuse including alcohol, cocaine, methamphetamines, marijuana, cigarette smoking, and opiates to a significantly higher extent than several types of active and inactive control groups. Moreover, MBIs can improve several psychological outcomes associated with drug consumption

Table A7: Summary of Findings of Included Studies	
Main Study Findings	**Author's Conclusions**
Bowen et al. 2014,[28] US, RCT	
Compared with TAU, participants assigned to MBRP reported significantly lower risk of relapse to substance use and heavy drinking and, among those who used substances, significantly fewer days of substance use and heavy drinking at the 6-month follow-up. RP showed an advantage over MBRP in time to first drug use. At the 12-month follow-up, MBRP participants reported significantly fewer days of substance use and significantly decreased heavy drinking compared with RP and TAU	RP and MBRP are beneficial aftercare interventions compared with typical 12-step aftercare treatment. MBRP also resulted in significantly less drug use and a lower probability of any heavy drinking than RP at a 12-month follow-up. These results suggest that MBRP may support longer term sustainability of treatment gains for individuals with substance use disorders

3S-therapy = Spiritual self-schema therapy; ABBT = Acceptance-Based Behavioral Therapy; ACT = Acceptance and Commitment Therapy; AR = Applied Relaxation; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; BDI-II = Beck Depression Inventory II; CBT = cognitive behavior therapy; CGI-S = Clinical Global Impression of Severity; CGI-I = Clinical Global Impression of Improvement; CSR = clinician's severity rating; DBT = Dialectical behavioral therapy; GAD = Generalized Anxiety Disorder; HAM-A = Hamilton Anxiety Rating Scale; HRQoL = Health-related quality of life; HRSD = Hamilton Rating Scale for Depression; MBCT = Mindfulness-Based Cognitive Therapy; MBCT-TS = MBCT with support to taper or discontinue antidepressant treatment; MBI = Mindfulness-based intervention; MBRP = Mindfulness-based relapse prevention; MBSR = Mindfulness-Based Stress Reduction; MD = major depression; MA = meta-analysis; NRT = Nicotine replacement therapy; PBCT = Person-Based Cognitive Therapy; PHQ-9 = The Patient Health Questionnaire-9; PTSD = post-traumatic stress disorder; QoL = Quality of Life; QOLI = Quality of Life Inventory; RCT = randomized controlled trial; RP = relapse prevention; SCL-90-R = Symptom Checklist-90-Revised; SIGH-A = Structured Interview Guide for the Hamilton Anxiety Rating Scale; SME = Stress Management Education; SR = systematic review; SUM = substance use and misuse; TAU = treatment as usual

Table A8: Summary of Findings of Included Studies
Main Study Findings
Post-traumatic stress disorder
The Management of Post-Traumatic Stress working group, 2010[34] – US Department of Veterans Affairs
• Complementary and alternative medicine such as mindfulness may be considered for adjunctive treatment of hyperarousal symptoms, although there is no evidence that these are more effective than standard stress inoculation techniques.   ○ The quality of evidence is poor, and the net benefit of the intervention is expected to range from zero or negative to substantial.
Depression
National Institute for Health & Clinical Excellence (NICE), 2010[9]
• Mindfulness-Based Cognitive Therapy is recommended for people who are currently well but have experienced three or more previous episodes of depression.   ○ The strength of recommendations is not graded in NICE guidelines
Scottish Intercollegiate Guidelines Network (SIGN), 2010[33]

• Mindfulness based cognitive therapy in a group setting may be considered as a treatment option to reduce relapse in patients with depression who have had three or more episodes.
  ○ A body of evidence including high quality systematic reviews of case control or cohort studies or high quality case control or cohort studies with a very low risk of confounding or bias, directly applicable to the target population, and demonstrating overall consistency of results; or
  ○ Extrapolated evidence from high quality meta-analysis, systematic reviews of RCTs or RCTs with low risk of bias

Parikh et al., 2009[32] – Canadian Network for Mood and Anxiety Treatments (CANMAT)
• Mindfulness-Based Cognitive Therapy is recommended as second-line therapy (cognitive behavioral therapy is first-line) for maintenance phase of major depressive disorders.   ○ Evidence based on at least 2 RCTs with adequate sample sizes, preferably placebo-controlled, and/or meta-analysis with narrow confidence intervals (level 2 of 4). • Cognitive behavior therapy and interpersonal therapy are the only first-line treatment recommendations for acute major depressive disorder and remain highly recommended for maintenance.
The Management of MDD working group, 2008[35] - US Department of Veterans Affairs
• Cognitive behavioral therapy, Cognitive Therapy, or Mindfulness-Based Cognitive Therapy (MBCT) should be used during the continuation phase of treatment with patients at high risk for relapse (i.e., two or more prior episodes, double depression, unstable remission status) to reduce the risk of subsequent relapse/recurrence.   ○ A strong recommendation that clinicians provide the intervention to eligible patients.
Substance use disorders
Mental Health and Drug and Alcohol Office, 2008[10] – New South Wales Department of Health
• Mindfulness-Based Stress Reduction can be used to treat problematic drug and alcohol use problems by suitably trained and experienced drug and alcohol professionals.   ○ The recommendation is supported by at least Level 3 research and expert clinical opinion (level 2 of 3)

MDD = major depressive disorder

APPENDIX 5: DETAILED DESCRIPTION OF STUDY INTERVENTIONS

Table A9: Detailed Description of Study interventions

Author, year	Interventions
Azad and Zadeh 2014,[24]	Mindfulness Intervention The experimental group received MBSR training. Eight 90-minute mindfulness training sessions were held twice a week and lasted for one month. The second session consisted of relaxation training for 14 muscle groups including forearm, calf, shin, thighs, abdomen, chest, shoulders, neck, lips, eyes, jaws, temples and forehead was done in second session. In the third session, relaxation training was received by participants. In addition. In forth session mindfulness-based breathing was introduced. Participants were trained to use the “inhale and exhale” technique with calmness and the “breath watching” technique. The participants were also asked to practice mindfulness-based breathing for 20 minutes before going to bed. In the fifth session, the participants were trained how to pay attention to body movements while breathing, to focus on body muscles and their movements, and to trace physical feelings, taste, hearing, etc. Mindfulness-based thinking was trained during session 6. Training sessions four, five and six were repeated for 20 to 30 minutes during session 7. The eighth session was a round-up session Control group No training
Omidi et al. 2013,[25]	Mindfulness Intervention Cognitive exercises and meditation techniques were taught in two-hour group sessions. Homework included meditation and other techniques on a daily basis during the 8 weeks Control group Treatment as usual, this group of patients continued their routine treatment without any more intervention.
Kearney et al. 2013,[31]	Mindfulness Intervention MBSR classes were taught by experienced instructors who met professional guidelines for teaching MBSR. 5 to 10 PTSD study subjects participated in each MBSR group. The MBSR groups met once weekly for 8 weeks (2.5 hours per session), plus a 7-hour session on a Saturday. Veterans practiced and received instructions on mindfulness meditation, discussed homework assignments, and had the opportunity to ask questions during each class. Between weeks six and seven of MBSR, the class met for a 7-hour session on a Saturday. Control group Treatment as usual, this group of patients continued to receive usual care for PTSD.
Kuyken et al. 2015,[21]	Mindfulness Intervention MBCT is intended to enable people to learn to become more aware of their bodily sensations, thoughts, and feelings associated with depressive relapse or recurrence and to relate constructively to these experiences. The program consisted of eight (2.25 hours group sessions), normally over consecutive weeks. Four refresher sessions were offered roughly every 3 months for the following year. Patients in the MBCT-TS group received support to taper or discontinue

Table A9: Detailed Description of Study interventions	
Author, year	**Interventions**
	their maintenance antidepressants both from the MBCT-TS therapist and their GPs. Control group Patients in the maintenance antidepressant group received support from their GPs to maintain a therapeutic level of antidepressant medication.
Meadows et al. 2014,[22]	Mindfulness Intervention After an initial individual orientation session, the MBCT program was delivered by an instructor in eight weekly 2-hour group training sessions involving up to ten participants. Sessions incorporated mindfulness practices and CBT-based exercises. Formal daily meditation practices and exercises for the development of everyday mindful awareness were included in the homework. DRAM was also used in addition to the MBCT, where DRAM comprised training on self-management of depression and supported monthly self-monitoring using The Patient Health Questionnaire-2 Control group DRAM
Chiesa et al. 2015,[23]	Mindfulness Intervention MBCT program comprised eight sessions of 2 hours each and was carried out by a psychiatrist psychotherapist and licensed MBCT instructor under the supervision of a clinical psychologist, psychotherapist and senior MBCT instructor. MBCT was carried out according to manualized procedures. The main changes concerned the investigation of current automatic thoughts rather than past automatic thoughts about MD and the integration of cognitive- behavioral exercises aimed to promote adaptive behaviors during current depressive episode rather than aimed at the prevention of future relapses. Control group The psychoeducation program comprised eight sessions of 2 hours each and was carried out by a clinical psychologist expert in the field of psychoeducational interventions. The sessions of the psychoeducation program were structured to be as similar as possible to those of MBCT, but emphasis was placed upon not describing or training mindfulness skills.
Tovote et al. 2014,[26]	Mindfulness Intervention The treatments were delivered individually in eight weekly sessions of 45–60 min. Patients were also instructed to do daily homework for 30 min. The central components of MBCT were formal meditation, yoga exercises, and informal daily mindfulness practices. Control group • CBT treatments were delivered individually in eight weekly sessions of 45–60 min. Patients were also instructed to do daily homework for 30 min. The main components of CBT were behavioral activation and cognitive restructuring. or • No psychological intervention for 3 months was received by participants in the waiting list condition.

Table A9: Detailed Description of Study interventions	
Author, year	**Interventions**
Bedard et al. 2014,[27]	Mindfulness Intervention Topics included meditation techniques, breathing exercises, gentle yoga, acceptance, awareness of thoughts and feelings, and staying in the present. The duration of the intervention was increased to 10 weeks (as opposed to the usual 8-week MBCT) with 90 minutes weekly sessions and a recommended daily meditation home practice for 20 to 30 minutes. Control group Waiting list
Hayes-Skelton et al. 2013,[29]	Both ABBT and AR treatments were 16 sessions in length, with four initial weekly 90 minute sessions followed by weekly 60 minute sessions and a biweekly taper between sessions 14, 15, and 16. Prior to session 1, therapists met with clients to learn more about the client's understanding of her/his worry and anxiety, to assess contextual factors that might affect the client's symptoms and course of therapy, to assess previous medication and therapy experiences, to briefly explore the client's cultural identity, to address any potential obstacles to treatment, and to instill hope. Mindfulness Intervention ABBT focuses on modifying problematic relationships with one's internal experiences. Each session began with a mindfulness exercise and a review of between session assignments, followed by the session specific content, and ending with the assignment of between session activities. ABBT has two distinct phases of treatment. The first phase (roughly sessions 1–7) introduced clients to an acceptance-based behavioral model of anxiety, focusing on the function of anxiety and emotions more broadly. Sessions in the second phase (roughly sessions 8–16) focused on applying the mindfulness and acceptance skills developed in the first phase of therapy as the client pursues valued life directions each week. Control group AR focuses on developing relaxation skills primarily through diaphragmatic breathing and progressive muscle relaxation.
Hoge et al. 2013,[30] USA	Mindfulness Intervention MBSR was comprised of eight weekly group classes (2 hours sessions) with a single weekend "retreat" day (4 hours), and daily home practice guided by audio recordings. In-class practices (breath-awareness, a body-scan, and gentle Hatha yoga) were used to cultivate awareness of internal present-moment experiences with an accepting, non-judgmental stance. Participants were also instructed in "informal" home mindfulness practice (e.g. present-focused awareness during eating, bathing, or cleaning) from 20 to 45 minutes. In addition, metta (loving-kindness) was introduced in the first class, and a metta CD for home practice was included Control group The SME course was designed as an active control, for comparison with MBSR, and did not contain any mindfulness components. It consisted of an 8-week two-hour class, with 20 minute homework exercises, and a 4-hour weekend class. The SME course was taught in a didactic format,

Table A9: Detailed Description of Study interventions	
Author, year	**Interventions**
	covering topics relevant to stress, stress physiology, effect of stress on body systems, sleep physiology, optimal nutrition, time management techniques, insomnia, effects of stress on diet, caffeine, exercise, stress hardiness, and factors that can buffer the impact of stress, such as humor, altruism, and volunteering.
Bowen et al. 2014,[28]	Mindfulness Intervention The MBRP intervention was composed of eight weekly, 2-hour sessions with 6 to 10 participants. Each session had a central theme, such as mindfulness in high risk situations, the role of "automatic pilot" in addiction, and balancing acceptance and action. All sessions included 20- to 30-minute guided meditations, experiential skills-based practices, and discussion of practical applications. Control group • RP intervention matched MBRP in time, size, format, location, and scope of assigned homework. Primary objectives included cognitive and behavioral coping skills, assessment of high risk situations, problem solving, goal setting, social support, and self-efficacy. Participants monitored daily craving and mood. or • The TAU program was abstinence based, and based on the Alcoholics/Narcotics Anonymous12- step program. Weekly groups included facilitated recovery-oriented discussions in an open-group format The TAU groups met 1 to 2 times weekly for 90 minutes.

ABBT = Acceptance-Based Behavioral Therapy; AR = Applied Relaxation; CBT = cognitive behavior therapy; DRAM = Depression Relapse Active Monitoring; MBCT = Mindfulness-Based Cognitive Therapy; MBCT-TS = MBCT with support to taper or discontinue antidepressant treatment ; MBRP = Mindfulness-based relapse prevention; MBSR = Mindfulness Based Stress reduction; PTSD = post-traumatic stress disorder; RP = relapse prevention

APPENDIX 6: Additional References of Potential Interest

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